

Sequence Listing

<110> Brunetta, Paul G. Sliwkowski, Mark X.

<120> THERAPY OF NON-MALIGNANT DISEASES OR DISORDERS WITH ANTI-ERBB2 ANTIBODIES

<130> P1979R1

<140> US 10/719,310

<141> 2003-11-21

<150> US 60/428,027

<151> 2002-11-21

<160> 22

<210> 1

<211> 107

<212> PRT

<213> Mus Musculus

<400> 1

Asp Thr Val Met Thr Gln Ser His Lys Ile Met Ser Thr Ser Val

1 5 10 15

Gly Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Ser 20 25 30

Ile Gly Val Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ser Pro Lys
35 40 45

Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp
50 55 60

Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
65 70 75

Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln 80 85 90

Tyr Tyr Ile Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu 95 100 105

Ile Lys

<210> 2

<211> 119

<212> PRT

<213> Mus musculus

<400> 2

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Thr Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Phe Thr Phe Thr Asp Tyr Thr Met Asp Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile Gly Asp Val Asn Pro Asn Ser Gly Gly Ser Ile Tyr Asn Gln Arg Phe Lys Gly Lys Ala Ser Leu Thr Val Asp Arg Ser Ser Arg Ile Val Tyr Met Glu Leu Arg Ser Leu Thr Phe Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asn Leu Gly Pro Ser Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser 110 <210> 3 <211> 107 <212> PRT <213> Artificial Sequence <223> sequence is synthesized <400> 3 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Ile Gly Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Ile Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu

Ile Lys

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<210> 4
<211> 119
<212> PRT
<213> Artificial Sequence
<223> sequence is synthesized
<220>
<221> artificial
<222> 1-119
<223> Fab 574 VH
<400> 4
Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly
Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr
 Asp Tyr Thr Met Asp Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 Glu Trp Val Ala Asp Val Asn Pro Asn Ser Gly Gly Ser Ile Tyr
 Asn Gln Arg Phe Lys Gly Arg Phe Thr Leu Ser Val Asp Arg Ser
 Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                                      85
 Thr Ala Val Tyr Tyr Cys Ala Arg Asn Leu Gly Pro Ser Phe Tyr
                                     100
 Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
                 110
                                     115
<210> 5
<211> 107
<212> PRT
<213> Artificial Sequence
<220>
<223> sequence is synthesized
<400> 5
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
                   5
Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser
 Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
```

Leu Leu Ile Tyr Ala Ala Ser Ser Leu Glu Ser Gly Val Pro Ser 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65 70 75

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln 80 85 90

Tyr Asn Ser Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu 95 100 105

Ile Lys

<210> 6

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> sequence is synthesized

<400> 6

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
1 5 10 15

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser

Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu 35 40 45

Glu Trp Val Ala Val Ile Ser Gly Asp Gly Gly Ser Thr Tyr Tyr
50 55 60

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
65 70 75

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp 80 85 90

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Arg Val Gly Tyr Ser Leu 95 100 105

Tyr Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser 110 115

<210> 7

<211> 10

<212> PRT

<213> Mus musculus

```
<220>
<221> unsure
<222> 10
<223> unknown amino acid
Gly Phe Thr Phe Thr Asp Tyr Thr Met Xaa
                   5
   1
<210> 8
<211> 17
<212> PRT
<213> Mus musculus
<400> 8
Asp Val Asn Pro Asn Ser Gly Gly Ser Ile Tyr Asn Gln Arg Phe
Lys Gly
<210> 9
<211> 10
<212> PRT
<213> Mus musculus
<400> 9
Asn Leu Gly Pro Ser Phe Tyr Phe Asp Tyr
<210> 10
<211> 11
<212> PRT
<213> Mus musculus
<400> 10
Lys Ala Ser Gln Asp Val Ser Ile Gly Val Ala
         . 5
   1
<210> 11
<211> 7
<212> PRT
<213> Mus musculus
<220>
<221> unsure
<222> 5-7
<223> unknown amino acid
<400> 11
 Ser Ala Ser Tyr Xaa Xaa Xaa
   1
<210> 12
<211> 9
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<212> PRT <213> Mus musculus <400> 12 Gln Gln Tyr Tyr Ile Tyr Pro Tyr Thr <210> 13 <211> 645 <212> PRT <213> human <400> 13 Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr Ala Leu Ala Val Leu Asp Asn Gly 110 115 Asp Pro Leu Asn Asn Thr Thr Pro Val Thr Gly Ala Ser Pro Gly 125 Gly Leu Arg Glu Leu Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys 140 145 Gly Gly Val Leu Ile Gln Arg Asn Pro Gln Leu Cys Tyr Gln Asp 155 Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser Ser Glu

200

Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys Ala 225 Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys 230 Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys 255 Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala 260 Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asp Pro 285 Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro 300 Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys 305 Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg 320 Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu 345 Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn 360 Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 380 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu 405 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 410 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Leu Gly Ile 440 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gln Cys Ile Gly Leu Gly Ile 440 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gln Cys Leu Gly Cys Lys Lys Ile Gly Gly Leu Gly Ile 440 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Gly Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Gly Ser Cry Leu His Asn Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Gly Ser Cry Leu Gly Leu Gly Ser Cry Leu His Asn Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Gly Cry Leu Gly Cry Cry Cry Cry Cry Cry Cry Cry Cry Cr															
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys 255 Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala 260 265 Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro 280 285 Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro 300 295 Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys 305 310 315 Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg 320 335 Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu 345 Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn 350 Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 365 Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala 390 Pro Leu Gln Pro Glu Gln Leu Gln Val The Glu Thr Leu Glu Glu 405 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 410 Asp Leu Ser Val Phe Gln Asn Leu Gln Cyl Leu Gly Leu Gly Leu Gly Leu 440 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Gly Leu 440 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Gly Leu 440 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Asp	Cys	Gln	Ser		Thr	Arg	Thr	Val		Ala	Gly	Gly	Cys	
Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala 270 Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro 285 Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro 300 Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys 315 Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg 320 Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu 345 Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn 360 Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 375 Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala 380 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 405 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 410 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 425 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile 445 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Arg	g Cys	Lys	Gly		Leu	Pro	Thr	Asp		Cys	His	Glu	Gln	_
Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro 285 Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro 300 Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys 315 Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg 320 Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu 345 Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn 360 Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 370 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 405 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 420 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Leu Gly Leu Gly Gle His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Ala	a Ala	Gly	Cys		Gly	Pro	Lys	His		Asp	Cys	Leu	Ala	
Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro 300 Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys 315 Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg 320 Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu 345 Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn 350 Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 380 Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala 380 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 405 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 410 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Leu Gly Ile 425 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Glu Gly Leu Gly Leu Gly Leu Gly Leu Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Lev	ı His	Phe	Asn		Ser	Gly	Ile	Cys		Leu	His	Cys	Pro	
Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys 315 Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg 320 Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu 345 Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn 360 Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 375 Phe Leu Pro Glu Ser Phe Asp Gly Asp 385 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 405 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 420 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 435 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Glu Gly Leu Gly Leu Gly Leu Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Let	ı Val	Thr	Tyr		Thr	Asp	Thr	Phe		Ser	Met	Pro	Asn	
Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg 320 Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu 345 Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn 355 Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 360 Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 370 Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala 380 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 405 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 420 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 435 Leu His Asn Gly Ala Tyr Ser Leu Trr Leu Gln Gly Leu Gly Ile 455 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Glı	ı Gly	Arg	Tyr		Phe	Gly	Ala	Ser	_	Val	Thr	Ala	Cys	
Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu 335 Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn 350 Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 370 Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala 380 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 400 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 410 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 425 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile 440 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Туг	Asn	Tyr	Leu		Thr	Asp	Val	Gly		Cys	Thr	Leu	Val	
Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn 360 Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 375 Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala 380 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 400 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 410 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 435 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile 440 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Pro) Leu	His	Asn		Glu	Val	Thr	Ala		Asp	Gly	Thr	Gln	-
Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala 375 Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala 380 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 400 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 415 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 425 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Leu Gly Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Суз	s Glu	Lys	Cys		Lys	Pro	Cys	Ala		Val	Cys	Tyr	Gly	
365 370 375 Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala 380 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 405 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 420 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 435 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile 445 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Gly	/ Met	Glu	His		Arg	Glu	Val	Arg		Val	Thr	Ser	Ala	
Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 405 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 415 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 425 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile 445 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Ile	e Gln	Glu	Phe		Gly	Cys	Lys	Lys		Phe	Gly	Ser	Leu	
Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 420 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 435 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gln Gly Leu Gly Ile 450 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Phe	e Leu	Pro	Glu		Phe	Asp	Gly	Asp		Ala	Ser	Asn	Thr	
Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 425 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile 440 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Pro) Leu	Gln	Pro		Gln	Leu	Gln	Val		Glu	Thr	Leu	Glu	
425 430 435 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile 440 445 450 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Ιlε	e Thr	Gly	Tyr		Tyr	Ile	Ser	Ala		Pro	Asp	Ser	Leu	
440 445 450 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu	Asp) Leu	Ser	Val		Gln	Asn	Leu	Gln		Ile	Arg	Gly	Arg	
	Let	ı His	Asn	Gly		Tyr	Ser	Leu	Thr		Gln	Gly	Leu	Gly	
455 460 465	Ser	Trp	Leu	Gly	Leu 455	Arg	Ser	Leu	Arg	Glu 460	Leu	Gly	Ser	Gly	Leu 465
Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val 470 475 480	Ala	a Leu	Ile	His		Asn	Thr	His	Leu		Phe	Val	His	Thr	

Pro	Trp	Asp ·	Gln	Leu 485	Phe	Arg	Asn	Pro	His 490	Gln	Ala	Leu	Leu	His 495
Thr	Ala	Asn	Arg	Pro 500	Glu	Asp	Glu	Cys	Val 505	Gly	Glu	Gly	Leu	Ala 510
Cys	His	Gln	Leu	Cys 515	Ala	Arg	Gly	His	Cys 520	Trp	Gly	Pro	Gly	Pro 525
Thr	Gln	Cys	Val	Asn 530	Cys	Ser	Gln	Phe	Leu 535	Arg	Gly	Gln	Glu	Cys 540
Val	Glu	Glu	Cys	Arg 545	Val	Leu	Gln	Gly	Leu 550	Pro	Arg	Glu	Tyr	Val 555
Asn	Ala	Arg	His	Cys 560	Leu	Pro	Cys	His	Pro 565	Glu	Cys	Gln	Pro	Gln 570
Asn	Gly	Ser	Val	Thr 575	Cys	Phe	Gly	Pro	Glu 580	Ala	Asp	Gln	Cys	Val 585
Ala	Cys	Ala	His	Tyr 590	Lys	Asp	Pro	Pro	Phe 595	Cys	Val	Ala	Arg	Cys 600
Pro	Ser	Gly	Val	Lys 605	Pro	Asp	Leu	Ser	Tyr 610	Met	Pro	Ile	Trp	Lys 615
Phe	Pro	Asp	Glu	Glu 620	Gly	Ala	Cys	Gln	Pro 625	Cys	Pro	Ile	Asn	Cys 630
Thr	His	Ser	Cys	Val 635	Asp	Leu	Asp	Asp	Lys 640	Gly	Cys	Pro	Ala	Glu 645